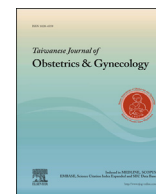


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Research Letter

Prenatal diagnosis of complete ring chromosome 22 without phenotypical abnormalities



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A healthy 34-year-old, para 1, Taiwanese woman presented for genetic amniocentesis at 18 weeks of gestation due to advanced maternal age. Her previous medical history was unremarkable except for a cesarean delivery following prolonged labor with a failed induction. Prenatal ultrasonography did not detect any structural abnormalities, except for borderline ventriculomegaly (Fig. 1). The karyotype of amniotic fluid cell culture was identified as 46,XY,r(22)(p13q13) (Fig. 2), which was further confirmed by cord blood sampling. Following detailed consultation and nondirective genetic counseling with physicians, the patient and her husband chose to terminate the pregnancy via hysterotomy. The procedure was performed uneventfully at 21 weeks of gestation. A dead male fetus weighing 520 g was delivered from breech presentation without any significant phenotypical abnormalities (Fig. 3) and no structural anomalies were found in an autopsy. Fetal skin and umbilical cord cultures were used to confirm the initial karyotype report postdelivery.

Ring chromosome 22 [r(22)] is a rare cytogenetic abnormality first identified by Weleber *et al* in 1968 [1]. Since that initial report, more than 60 cases have been described in medical literature. Ring chromosomes usually occur when a terminal break in both arms of the chromosome and the broken ends fuse together, or one broken chromosome end joins with the opposite telomeric region. This condition results in the loss of genetic material. Alternatively, ring chromosomes can be formed by the fusion of subtelomeric sequences or telomere-telomere fusion with no deletion, resulting in complete ring chromosomes. Ring chromosomes often lead to developmental anomalies but are

rarely inherited. The presence of an r(22) is usually associated with a phenotype that is difficult to define clinically. The only consistent observation with r(22) is moderate to severe mental retardation. Other frequently reported symptoms include muscular hypotonia, poor coordination (unsteady gait), hyperactivity, microcephaly, and nonspecific dysmorphic features. The variability of this phenotype is believed to result from the instability of the ring chromosome rather than the extent of the deletion at 22q13.3. Additionally, loss of 22q13.3 is sometimes considered to be a simple terminal deletion. Phenotypes associated with the 22q13.3 deletion syndrome are developmental delay, normal to accelerated growth, severe delay in expressive speech, hypotonia, and mild dysmorphic features. Neither the r(22) nor the 22q13.3 deletion syndromes are associated with serious malformations [2].

Only a few cases of r(22) have been diagnosed prenatally. Searching the keywords “prenatal diagnosis” and “ring

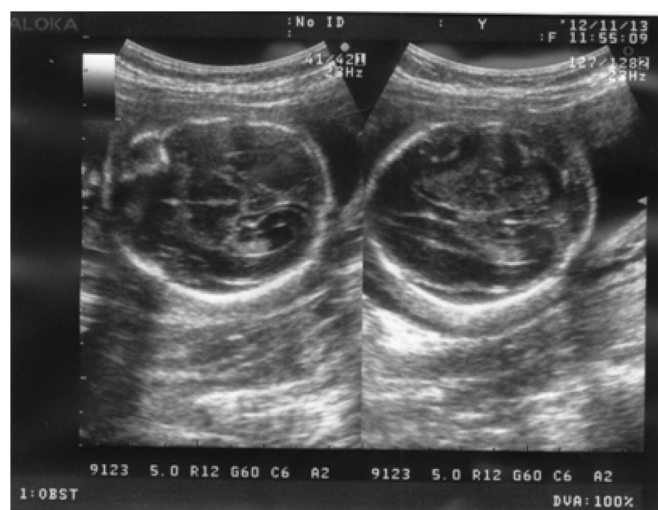


Fig. 1. Prenatal ultrasound images showing borderline ventriculomegaly.

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Fig. 2. Amniotic fluid cell culture karyotype showing ring chromosome 22.



Fig. 3. Stillborn fetus showed no significant phenotypic abnormalities.

Table 1

Reported cases of prenatally diagnosed ring chromosome 22.

Author	Indication	Fetal sex	Gestational age	Ring chromosome 22	Phenotype anomalies
Chen et al, 2003 [3]	Advanced maternal age	Female	18 wk	Mosaic ^a <i>de novo</i>	Cardiovascular abnormalities and IUGR
Declán et al, 2004 [4]	Voluntary	—	16 wk	Deletion 22q13.3 <i>de novo</i>	Agenesis of corpus callosum, fornix, and septum pellucidum
McClarren et al, 2006 [5]	Cystic hygroma	—	12 wk	Deletion 22q11.2	Truncus arteriosus and thymic hypoplasia
		Male		Maternally inherited	
Koç et al, 2009 [6]	Abnormal screening	Female	First trimester	Mosaic ^b <i>de novo</i>	Choroids plexus cyst
Gadji et al, 2011 [7]	Advanced maternal age	Male	16 wk	Two constitutional rings ^c	Low set ear, hypertelorism, bilateral clinodactyly 5 th finger, and 13 rib pair
Present case	Advanced maternal age	Male	18 wk	r(22)(p13q13)	No major abnormalities

IUGR = intrauterine growth restriction.

^a 45,XX, -22[6]/46,XX,r(22)(p13q13.31)[15].

^b Duplication/deletion 22q 13.

^c 47,XY,r(22)(p11.1p11.2),+r(22) (q11.1q13.31).

chromosome 22" on the PubMed database yielded four case reports of r(22) [3–6]. There was also an additional report of two constitutional rings derived from a single chromosome 22 [7]. These reports, as well as the case identified in this report, are summarized in

Table 1. The mutations and phenotypes associated with each reported case of r(22) are different. In conclusion, the ring chromosome 22 disorder generally arises from *de novo* genetic mutations and leads to a variable phenotypic spectrum.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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